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(56) Documents Cited
WO 93/25189 A **WO 92/11839 A** **WO 91/01712 A**
US 5167950 A
Abstract of DE 2807929

(58) Field of Search
UK CL (Edition P) **A5B BLC**
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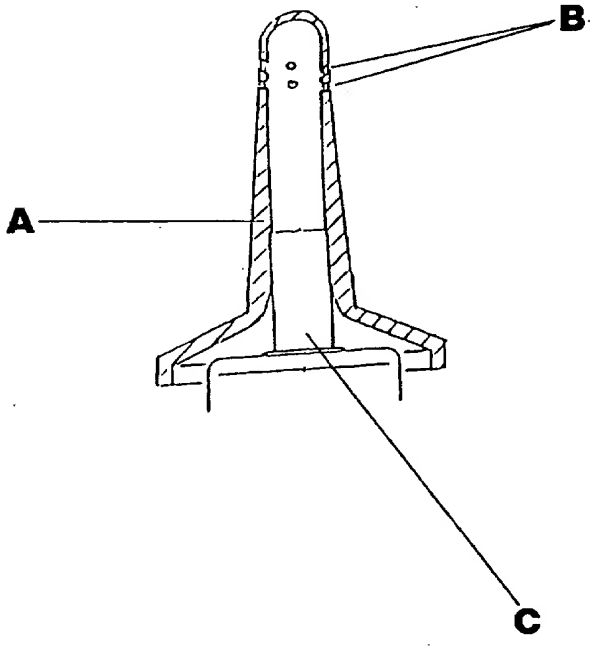
(54) Abstract Title
Nasal antiseptic compositions

(57) The aerosol composition comprises an antiseptic an emulsion and a propellant.
The antiseptic is preferably triclosan or chlorhexidine gluconate.
The emulsion is preferably an oil/water emulsion and contains sorbitan tristearate, polyethylene glycol and iso-propyl myristate.



A = Body of the nozzle.

B = Orifices at angles through which foam passes.

C = The aerosol valve stem to which the nozzle is attached.

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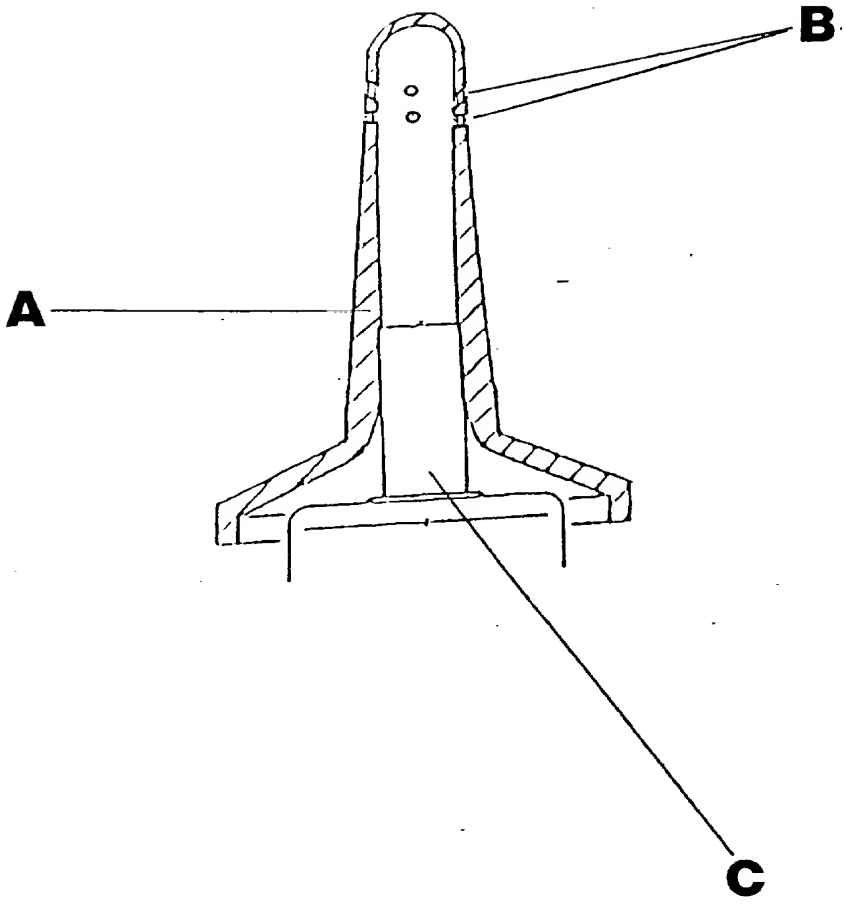
B
A
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DRAWING

A = Body of the nozzle.

B = Orifices at angles through which foam passes.

C = The aerosol valve stem to which the nozzle is attached.

NASAL ANTISEPTIC COMPOSITIONS

This invention concerns antiseptic compositions containing an active ingredient dispensed from a pressurised container and specifically
1 designed and formulated for application to the nasal passage, in the form of a foam.

There are many infected conditions of the nose for which a variety of methods for applying an antibacterial preparation exist. Such methods are also used for infections arising from, fungi, yeasts or
2 viruses. Presentations of preparations to combat infections of the nasal passages are commonly in the form of a liquid, a cream or an ointment.

These current presentations of nasal compositions have the following
3 disadvantages in the clinical management of nasal infections:

1.

They do not provide a regulated dose of an anti-infective agent, for example the smearing of a cream or ointment or the douching of a liquid leaves the level of active agent getting into the nasal passage to
4 the random choice of the amount of liquid, cream or ointment used by the user or person applying the preparation. A particular problem with liquids is that they can run out of the nose before the active agent has been in contact with an infected surface for sufficient time to be effective.

They present particular problems in coming into contact and remaining in contact with surfaces of the nasal passages. Such surfaces being for example skin, mucous membranes or hairs. Liquids can miss making contact with an area needing treatment or run out of the nose before having time for the active agent to be effective.

Creams and ointments can be too viscous to ensure an adequate dispersion within the nasal passages when smeared onto internal surfaces, using a finger or suitable instrument.

Application into the nasal passage of such preparations involves the use of fingers or implements, which may themselves be carrying potentially harmful bacteria or organisms. Ideally the preparation would be applied into the nasal passages using a sterilised instrument or in such a manner that would avoid the risk of further infecting the nasal passages.

According to the present invention there is provided a pressurised container or aerosol, containing a suitable anti-infective formulation of ingredients and propellant, having a metered dose aerosol valve and spray nozzle, which upon being actuated releases a single predetermined quantity emission of foam. When the aerosol valve is released and returns by the action of an internal spring system to its original position, the process of actuation can be repeated.

Such a presentation of an active ingredient in the form of a metered
9 foam would be particularly useful for the treatment of nasal infections. It would have the following advantages: -

1.

The contents of the pressurised aerosol are protected from the chance
10 contamination by airborne bacteria or other organisms such as fungi, yeasts and viruses.

2.

The action of the aerosol metered valve system provides a method of
11 applying a prescribed dose of foam and therefore the anti-infective agent, which it contains.

3.

The foam can be administered directly into the nasal vestibule avoiding carrying potentially harmful organisms into an already
12 infected area, which could arise from contact with an instrument or finger as described when applying a cream or ointment.

4.

The foam, formed from the aerosol propellant rapidly changing from liquid under pressure to a gaseous form when released into the atmosphere by operation of the aerosol valve, continues to expand
13 due to the warm environment of the nasal passage. This expansion assists penetration of the preparation on to the infected internal surfaces of skin, mucous membrane and hairs, within the nasal passage.

A foam can be more readily spread within the nasal vestibule by external massage of the soft tissue of the nose, compared to the use of a viscous cream or ointment. The action of external massage further
14 provokes expansion of the foam arising from the resultant increased direct contact with the internal nasal surfaces at body temperature. The increase in temperature of the foam causes the minute bubbles of gaseous aerosol propellant trapped in the preparation to expand, thus increasing the total volume of foam in the nasal passage.

The invention would be particularly of benefit in the treatment of persons infected with or being carriers of bacteria that are resistant to
15 one or more antibiotics. A carrier is a person who has the bacteria on their body, but are not suffering any direct adverse effect or illness from its presence.

An example of an antibiotic resistant strain of bacteria is Methicillin Resistant Staphylococcus Aureus, often referred to as
16 MRSA. Hospitals report three strains, referred to as Endemic MRSA-3, EMRSA-15 and EMRSA-16.

These resistant organisms pose a threat to the development of other organisms becoming resistant to other antibiotics. As resistant strains
17 appear, the medical profession loses the future use of the antibiotic involved in combating infectious diseases.

The Methicillin Resistant Staphylococcus Aureus (MRSA) can be found
18 anywhere on the body of a carrier or infected person, but is most frequently found in the nasal vestibule.

Treatment involves isolation of the patient and frequent whole body
19 washing with a suitable antiseptic preparation. The nasal vestibule is treated with an ointment or cream, applied using the fingertips or a suitable instrument.

This invention provides an improved method of applying an antiseptic to the nasal vestibule of a person whose nose is infected with antibiotic
20 resistant bacteria, where contamination by micro-organisms from using fingertips or instruments to smear a cream or ointment is avoided.

A suitable antiseptic is Triclosan (2,4,4-trichloro-2-hydroxy diphenyl
21 ether) or Chlorhexidine (1,1-Hexamethylenebis {5-(4-chlorophenyl) biguanide} or Polyvinyl Pyrrolidone Iodine.

Triclosan and Chlorhexidine are particularly useful because they are
22 very active against gram-positive bacteria e.g. Staphylococcus Aureus and are substantive to the skin, having a remanent effect.

An example of a suitable formulation would be the antiseptic Triclosan or Chlorhexidine dissolved in an oil in water emulsion. This
23 emulsion is then filled into a suitable aerosol container, sealed with a suitable metering aerosol valve, followed by the injection of a suitable propellant.

Example 1: - Preparation of oil in water emulsion comprising Triclosan.
Percentages refer to percentages w/v of the final emulsion.

Triclosan	1.0%
Sorbitan Tristearate	4.5%
Polyethylene Glycol	20.0%
Iso Propyl Myristate	5.0%
Benzyl Alcohol	0.3%
Purified Water	69.2%

Example 2: - Preparation of oil in water emulsion comprising Chlorhexidine.

Chlorhexidine Gluconate	1.0%
Sorbitan Tristearate	4.5%
Polyethylene Glycol	20.0%
Iso Propyl Myristate	5.0%
Benzyl Alcohol	0.3%
Purified Water	69.2%

An emulsion of the invention may be prepared by methods well known to those skilled in the art. For example it may be prepared by
24 heating the oils to 70°C, then adding them steadily to the water phase (also at 70°C) with good stirring then allowing the emulsion to cool.

Example of an aerosol formulation: -

Product (for example formulations 1 or 2)	95%
Propellant	5%

Examples of a propellant would be Butane, Iso Butane, Propane,
25 Dichlorodifluoromethane, Trichlorofluoromethane, Dimethylether. Propellants can be a single substance or a mixture of substances.

The aerosol valve would be fitted with a nozzle or an actuator. It
26 would be preferred that the nozzle is sufficiently narrow to fit into the nasal vestibule, so releasing a metered dose of foam inside the nose.

It would also be preferred that the nozzle emits foam in a direction horizontal to the direction it is pointing, as indicated in the drawing.

CLAIMS

1. An aerosol spray composition comprising an antiseptic, an emulsion, a propellant, an aerosol valve and nozzle designed to deliver a dosage of foam to the nasal vestibule.

2. An aerosol as in claim 1 fitted with a metering valve to deliver a dose of its contents of 5mg to 500mg upon each actuation.

3. An emulsion as in claim 1 wherein the emulsion is an oil in water emulsion.

4. An emulsion as in claim 3 wherein the oil in water emulsion is formed, by an emulsifying agent with surfactant properties.

5. An emulsion as in claim 3 wherein the surfactant emulsifying agent is a Sorbitan Derivative such as Sorbitan Tristearate.

6. An emulsion as in claim 3 wherein the emulsifying agent is a mixture of aliphatic alcohols such as Stearyl or Cetyl Alcohol.

7. An emulsion as in claim 1 containing an isopropyl fatty acid ester for example iso propyl myristate.

8. An emulsion as in claim 1 containing a Macrogol, for example Polyethylene Glycol.

9. A composition as in claim 1 wherein the antiseptic is selected from Triclosan, Chlorhexidine, Polyvinylpyrrolidone-Iodine, Hexachlorophane, Domiphen Bromide and other quarternary ammonium disinfectants, Noxythiolin, Polynoxylin and Dequalinium Chloride.

10. A composition as in claim 1 wherein the antiseptic is an antibiotic.

11. A composition as in claim 1 containing a preservative selected from Benzyl Alcohol, Chlorocresol, Cresol, Hydroxybenzoates Phenethyl Alcohol, Benzalkonium Chloride, Chlorbutol and Cetrimide.

12. A composition as in claim 1 wherein the propellant is selected from one or more of Butane, Iso-Butane, Propane, Dichlorodifluoromethane, Trichlorofluoromethane, Dimethylether.

13. An emulsion according to any one of claim 1 to 11 consisting essentially of:-

Sorbitan Tristearate	0.5 to 7% w/v
Polyethylene Glycol	1.0 to 30% w/v
Iso propyl myristate	1.0 to 10% w/v
Triclosan	0.1 to 5% w/v
Benzyl Alcohol	0.1 to 1% w/v
Purified water	to 100% w/v of the emulsion

14. An aerosol according to any one of claims 1 to 12 consisting essentially of:

Emulsion with antiseptic	1 to 40% w/w
Butane	1 to 40% w/w
Propane	1 to 20% w/w

15. A composition as in claim 1 wherein the aerosol actuator or nozzle is designed to be able to enter the nasal vestibule.

16. A composition as in claim 12 wherein the aerosol actuator or nozzle can be activated to release a dose of foam into the nasal vestibule.

17. A composition as in claim 1 wherein the aerosol actuator or nozzle releases a dose of foam in a direction which is at varying angles to the axis of the nozzle.

18. A composition as in claim 4 wherein the design of a nozzle is set out in the drawing.

19. An aerosol composition substantially as herein described for use in medicine for the treatment of infections to the nasal passages.

The Patent Office

Application No:	GB 9813626.0	**Examiner:**	Diane Davies
Claims searched:	1-19	**Date of search:**	14 October 1998

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.P): A5B: BLC

Int Cl (Ed.6): A61K 9/00, 9/12

Other: Online:EDOC, JAPIO, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	WO 9325189 A	(Ballard medical Products *et al*) Whole document: antibiotic formulation for topical application as a foam in an aerosol dispensing system having an emulsion and propellant.	1-19
X	WO 9211839 A	(L. Mackles & L. Chavkin) Whole document: aerosol foam composition comprising a foaming agent and propellant together with an active ingredient which may be an antibiotic or antimicrobial agent.	1-19
X	WO 9101712 A	(Hisamitsu Pharmaceutical Co. Ltd.) Whole document: foamed aerosol composition containing surfactant, alcohol or water and propellant as well as, for example, an antibacterial agent.	1-19
X	US 5167950 A	(Johnson & Son Inc.) Whole document: aerosol mousse containing an anti-microbial for dispensing as a foam for use as an antiseptic.	1-19

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

The Patent Office

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Application No: GB 9813626.0
Claims searched: 1-19

Examiner: Diane Davies
Date of search: 14 October 1998

Category	Identity of document and relevant passage	Relevant to claims
X	Abstract of DE 2807929 A (F. Torossian) Foam-forming composition for administration to the nasal cavity.	At least claim 1

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.